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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/556,641	11/06/2006	Sandrine Salle	REGIM 3.3-069	8511
530	7590	09/11/2008	EXAMINER	
LERNER, DAVID, LITTENBERG, KRUMHOLZ & MENTLIK 600 SOUTH AVENUE WEST WESTFIELD, NJ 07090			WESTERBERG, NISSA M	
ART UNIT	PAPER NUMBER			
		1618		
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/556,641	<b>Applicant(s)</b> SALLE ET AL.
	<b>Examiner</b> Nissa M. Westerberg	<b>Art Unit</b> 1618

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(o).

#### Status

- 1) Responsive to communication(s) filed on \_\_\_\_\_.
- 2a) This action is FINAL.      2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-7 is/are pending in the application.
  - 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_ is/are allowed.
- 6) Claim(s) 1-7 is/are rejected.
- 7) Claim(s) \_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) All    b) Some \* c) None of:
    1. Certified copies of the priority documents have been received.
    2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement (PTO/SB/08) \_\_\_\_\_  
 Paper No(s)/Mail Date \_\_\_\_\_
- 4) Interview Summary (PTO-413)  
 Paper No(s)/Mail Date \_\_\_\_\_
- 5) Notice of Informal Patent Application
- 6) Other: \_\_\_\_\_

**DETAILED ACTION**

***Comments and Notes***

On the bottom of page 2 of the declaration, the box indicating additional inventors has been checked but the line for the number of supplemental Additional Inventor sheets has been left blank. While two inventors on the declaration matched the inventors listed on the Application Data Sheet, the Oath/Declaration controls for the citizenship and the naming of the inventors. Given the checked box but uncompleted blank, a question could arise as to whether all of the inventors are listed and have signed the declaration.

***Claim Rejections - 35 USC § 112 1<sup>st</sup> Paragraph***

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1 – 7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. None of the water-insoluble alkyl cellulose

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ether derivatives water-insoluble acrylic polymer derivatives and water-insoluble vinyl derivatives other than those examples provided on p 4, ln 19 – 24 meet the written description provision of 35 USC § 112, first paragraph, due to lacking chemical structural information for what they are and chemical structures are highly variant and encompass a myriad of possibilities. The specification provides insufficient written description to support the genus of derivatives encompassed by the claim, since there is no description of the structural relationship of these derivatives provided in the specification and Applicant has not provided a description as to how the base molecule may be changed while remaining a water-insoluble derivative of the polymer.

***Claim Rejections - 35 USC § 112 2<sup>nd</sup> Paragraph***

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1 – 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The first film layer contains a “relatively water-insoluble macromolecular substance”. “Relatively” is a relative which renders the claim indefinite. The term “relatively” is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Examples are given

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in the specification on p 4, ln 14 – 24 but the definition given seems to indicate that “relatively water-insoluble substances” are water insoluble but the use of the word relatively seems to indicate that a substance with some degree of water solubility would also be included within the scope of the claims.

5. Claims 1 – 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The second skin layer contains “one or more hot-melt low-melting substances”. The description of these ingredients appears contradictory in that they melt at hot temperatures which implies a high temperature, although no standard with which to judge “hot” is provided, but yet melt at a “low temperature”. A non-limiting definition is given on p 4, ln 25 – 28 which uses the undefined relative term of “a substance having a relatively low melting point”. Preferred examples with specific temperatures are given, but it does not constitute a limiting definition of the term. Examples of specific substances are provided from p 4, ln 29 – p 5, ln 10. In the absence of a limiting definition in the specification, what substances would meet these criteria and which would not is not defined and therefore the claims are vague and indefinite.

6. Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Step d) of the method is “curing said coated granules to form

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films". For this step, one could form the granules into a flat, three dimensional film of material. The granules could also have film coated layers applied to them which were then cured. Step e), in which the coated granules are encapsulated, in a capsule, the granules could be separate granules with a film-coating applied or the film of material could be rolled up and placed inside of the capsule.

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1 – 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hara et al. (JP 02225416A; CAPLUS Abstract) and further in view of Samejima et al. (US 5,068,112) and Maruyama et al. (US 5,837,291).

Hara et al. discloses oral preparation of compound I, beraprost sodium, in which granules of active ingredient, lactose and corn starch are coated with EUDRAGIT® S-100 and dried. The application of the enteric coating results in a larger area under the curve (AUC) for beraprost sodium when the granules are administered to dogs.

Hara et al. does not disclose the sizes of the granules or the encapsulation of the granules into a capsule. Hara et al. also does not disclose the presence of a second coating containing one or more hot-melt low-melting substances.

Samejima et al. discloses a core to be coated with a porous film with a preferred granule size of about 300 µm to about 2000 µm, preferably about 500 µm to about 850 µm (col 2, ln 6 – 16). The porous film material can be hydrophobic and insoluble in water (col 2, ln 37 – 61) or an enteric polymer such EUDRAGIT® L or S (col 3, ln 14 – 42). The thickness and porosity of the film allows for control of the dissolution rate (col 4, ln 60 – col 5, ln 3). The obtained pharmaceutical preparation can be administered in

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the form of filled capsules when the preparation is in the shape of granules (col 6, ln 32 – 36).

Maruyama et al. discloses that the hydrophobic waxes including higher alcohols, higher fatty acids and glycerine fatty acid esters in conjunction with an enteric coating improves the water resistance of the obtained enteric preparation (col 2, ln 66 – col 3, ln 3).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to prepare the enteric beraprost sodium granules as taught by Hara et al. to increase the bioavailability of the beraprost sodium and to add a wax coating such as the higher alcohols, higher fatty acids or glycerine fatty acid esters, exemplified by applicant as hot melt low melting substances to improve the water resistance of the enteric coating preparation, as taught by Maruyama et al. As to the size of the granules, Samejima et al. teaches that granule sizes of less than 1000 µm are suitable for enteric coated granules such as those described by Hara et al. and those coated granules can be used to fill a capsule to make an oral sustained release composition, as required in claim 6. In regards to ratio of the first a second coating layers, Maruyama et al. discloses that the porosity and thickness of the layer, both of which are reflected to some degree by the absolute weight of the layer, alters the dissolution profiled of the core and the active ingredient contained therein. The amount of each of these layers is a results effective parameter that determines the release profile of active ingredient from the pharmaceutical compositions. Optimization of parameters is a routine practice that

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would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success.

11. Claims 1 – 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hara et al. (JP 02225416A; CAPLUS Abstract) and further in view of Samejima et al. (US 5,068,112) and Gowan, Jr. et al. (US 5,405,617).

Hara et al. discloses oral preparation of compound I, beraprost sodium, in which granules of active ingredient, lactose and corn starch are coated with EUDRAGIT® S-100 and dried. The application of the enteric coating results in a larger area under the curve (AUC) for beraprost sodium when the granules are administered to dogs.

Hara et al. does not disclose the sizes of the granules or the encapsulation of the granules into a capsule. Hara et al. also does not disclose the presence of a second coating containing one or more hot-melt low-melting substances.

Samejima et al. discloses a core to be coated with a porous film with a preferred granule size of about 300 µm to about 2000 µm, preferably about 500 µm to about 850 µm (col 2, ln 6 – 16). The porous film material can be hydrophobic and insoluble in water (col 2, ln 37 – 61) or an enteric polymer such EUDRAGIT® L or S (col 3, ln 14 – 42). The thickness and porosity of the film allows for control of the dissolution rate (col 4, ln 60 – col 5, ln 3). The obtained pharmaceutical preparation can be administered in the form of filled capsules when the preparation is in the shape of granules (col 6, ln 32 – 36).

Gowan, Jr. et al. discloses a taste mask coating or carrier matrix for pharmaceutical preparations comprising an aliphatic or fatty acid ester which should be a solid at room temperature (col 2, ln 22 – 36). In example 2 (col 6, ln 46 – 57), granules of acetaminophen were sprayed with a melted solution of stearyl stearate to provide individual crystals or granules coated for taste masking by this method. The ratio of drug to coating ratio is generally between about 5:95 and 50:50, the higher ratios being particularly useful for swallowable dosage forms where taste masking isn't required (col 5, ln 13 – 23).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to take the enteric beraprost granules taught by Hara et al. to increase the bioavailability of the active ingredient and to coat them with a aliphatic or fatty acid ester to produce a taste masked pharmaceutical composition as taught by Gowan, Jr. et al. As to the size of the granules, Samejima et al. teaches that granule sizes of less than 1000  $\mu\text{m}$  are suitable for enteric coated granules such as those described by Hara et al. and those coated granules can be used to fill a capsule to make an oral sustained release composition, as required in claim 6. In regards to ratio of the first a second coating layers, Gowan, Jr. et al. discloses that the amount of the applied layer depends on the intended application of the granules. The amount of each of these layers is a results effective parameter that determines the release profile of active ingredient from the pharmaceutical compositions. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8 a.m. - 4 p.m. ET. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/  
Supervisory Patent Examiner, Art Unit 1618

NMW